Amendments to the Specification:

Please replace the paragraph at lines 1-8 on page 3 with the following paragraph:

In certain preferred embodiments, the cell is engineered with (i) a recombinant gene encoding a Dicer activity, (ii) a recombinant gene encoding an Argonaut activity, or (iii) both. For instance, the recombinant gene may encode, for a example, a protein which includes an amino acid sequence at least 50 percent identical to SEQ ID ~~No.~~ NO: 2 or 4; or be defined by a coding sequence hybridizes under wash conditions of 2 x SSC at 22°C to SEQ ID ~~No.~~ NO: 1 or 3. In certain embodiments, the recombinant gene may encode, for ~~a~~ example, a protein which includes an amino acid sequence at least 50 percent identical to the Argonaut sequence shown in Figure 24.

Please replace the paragraph at lines 12-20 on page 6 with the following paragraph:

Figure 1: RNAi in S2 cells. ~~a,~~ 1A. *Drosophila* S2 cells were transfected with a plasmid that directs *lacZ* expression from the copia promoter in combination with dsRNAs corresponding to either human CD8 or lacZ, or with no dsRNA, as indicated. ~~b,~~ 1B. S2 cells were co-transfected with a plasmid that directs expression of a GFP–US9 fusion protein (12) and dsRNAs of either *lacZ* or *cyclin E,* as indicated. Upper panels show FACS profiles of the bulk population. Lower panels show FACS profiles from GFP-positive cells. ~~c,~~ 1C. Total RNA was extracted from cells transfected with *lacZ, cyclin E, fizzy* or *cyclin A* dsRNAs, as indicated. Northern blots were hybridized with sequences not present in the transfected dsRNAs.

Please replace the paragraph at lines 21-33 on page 6 with the following paragraph:

Figure 2: RNAi *in vitro*. ~~a,~~ 2A. Transcripts corresponding to either the first 600 nucleotides of *Drosophila cyclin E* (E600) or the first 800 nucleotides of *lacZ* (Z800) were incubated in lysates derived from cells that had been transfected with either *lacZ* or *cyclin E* (cycE) dsRNAs, as indicated. Time points were 0, 10, 20, 30, 40 and 60 min for *cyclin E* and 0, 10, 20, 30 and 60 min for *lacZ*. ~~b,~~ 2B. Transcripts were incubated in an extract of S2 cells that had been transfected with *cyclin E* dsRNA (cross-hatched box, in 2D below). Transcripts corresponded to the first 800 nucleotides of *lacZ* or the first 600, 300, 220 or 100 nucleotides of

cyclin E, as indicated. Eout is a transcript derived from the portion of the *cyclin E* cDNA not contained within the transfected dsRNA. E-ds is identical to the dsRNA that had been transfected into S2 cells. Time points were 0 and 30 min. ~~e,~~ 2C. Synthetic transcripts complementary to the complete *cyclin E* cDNA (Eas) or the final 600 nucleotides (Eas600) or 300 nucleotides (Eas300) were incubated in extract for 0 or 30 min.

Please replace the paragraph at lines 6-14 on page 7 with the following paragraph:

Figure 4: The RISC contains a potential guide RNA. ~~a,~~ 4A. Northern blots of RNA from either a crude lysate or the S100 fraction (containing the soluble nuclease activity, see Methods) were hybridized to a riboprobe derived from the sense strand of the *cyclin E* mRNA. ~~b,~~ 4B. Soluble *cyclin-E*-specific nuclease activity was fractionated as described in Methods. Fractions from the anion-exchange resin were incubated with the lacZ, control substrate (upper panel) or the cyclin E substrate (centre panel). Lower panel, RNA from each fraction was analysed by northern blotting with a uniformly labelled transcript derived from sense strand of the *cyclin E* cDNA. DNA oligonucleotides were used as size markers.

Please replace the paragraph bridging pages 8 and 9 with the following paragraph:

Figure 8: Dicer is an evolutionarily conserved ribonuclease. A. A model for production of 22mers by Dicer. Based upon the proposed mechanism of action of Ribonuclease III, we propose that Dicer acts on its substrate as a dimer. The positioning of the two ribonuclease domains (RIIIa and RIIIb) within the enzyme would thus determine the size of the cleavage product. An equally plausible alternative model could be derived in which the RIIIa and RIIIb domains of each Dicer enzyme would cleave in concert at a single position. In this model, the size of the cleavage product would be determined by interaction between two neighboring Dicer enzymes. B. Comparison of the domain structures of potential Dicer homologs in various organisms (*Drosophila* - CG4792, CG6493, *C. elegans* - K12H4.8, *Arabidopsis* – CARPEL FACTORY[24], T25K16.4, AC012328_1, human Helicase-MOI[25] and *S. pombe* - YC9A_SCHPO). The ZAP domains were identified both by analysis of individual sequences with Pfam[27] and by Psi-blast[28] searches. The ZAP domain

in the putative *S. pombe* Dicer is not detected by PFAM but is identified by Psi-Blast and is thus shown in a different color. For comparison, a domain structure of the RDE1/QDE2/ARGONAUTE family is shown. It should be noted that the ZAP domains are more similar within each of the Dicer and ARGONAUTE families than they are between the two groups. ~~C. An alignment of the ZAP domains in selected Dicer and Argonaute family members is shown. The alignment was produced using ClustalW.~~

Please replace the paragraph at lines 32-35 on page 9 with the following paragraph:

Figure 20: Identification of dicer as enzyme which can process dsRNA into 22mers. Various RNaseIII family members were expressed with n terminal tags, immunoprecipitated, and assayed for 22mer generating activity (20A, left panel). In right panel (20C), antibodies to dicer could also precipitate 22mer generating activity. Diagrammatic representations of the domain structures of CG4792/Dicer-1, Drosha and Homeless are shown in 20B (also shown as Figure 6B).

Please replace the paragraph at line 2 on page 10 with the following paragraph:

Figure 22 (20A and 20B): Dicer produces RNAs that are the same size as RNAs present in RISC.

Please replace the paragraph at lines 14-23 on page 17 with the following paragraph:

In certain embodiment, at least one of the activated RNAi enzymes is Dicer, or a homolog thereof. In certain preferred embodiments, the present method provides for ectopic activation of Dicer. As used herein, the term "Dicer" refers to a protein which (a) mediates an RNAi response and (b) has an amino acid sequence at least 50 percent identical, and more ~~preferablty~~ preferably at least 75, 85, 90 or 95 percent identical to SEQ ID ~~No.~~ NO: 2 or 4, and/or which can be encoded by a nucleic acid which hybridizes under wash conditions of 2 x SSC at 22°C, and more preferably 0.2 x SSC at 65°C, to a nucleotide represented by SEQ ID ~~No.~~ NO: 1 or 3. Accordingly, the method may comprise introducing a dsRNA ~~contruct~~ construct into a cell in which Dicer has been recombinantly expressed or otherwise ectopically activated.